

**Amendment and Response**

Applicant: Winthrop D. Childers et al.

Serial No.: 10/808,945

Filed: March 25, 2004

Docket No.: 200314152-1

Title: METHOD OF SORTING CELLS ON A BIODEVICE

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**REMARKS**

The following remarks are made in response to the Office Action mailed October 23, 2007, in which claims 1-4, 7, 14, 15, 18 and 21-24 were rejected, and claims 5, 6, 8-13, 16, 17, 19, 20 and 25-29 were indicated to be allowable if rewritten into proper form. With this Response, claims 1, 4-8, 10, 12-16, 18-20, 22, 23, and 25-28 have been amended. Claims 1, 4-20, and 22-28 remain pending in the application and are presented for reconsideration and allowance.

**Objection to the Specification**

Applicants have amended the specification to include the missing serial numbers of the related applications.

**Claim Rejections under 35 U.S.C. § 112**

In the Office Action, claims 21 and 22 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. However, claims 21 and 22 were further indicated to be allowable if rewritten to overcome the Section 112 rejection and to incorporate the limitations of any base and intervening claims.

Accordingly, Applicants have canceled claim 21 and amended independent claim 14 to incorporate the limitations of claim 21 while also addressing the Section 112 rejection. In particular, independent claim 14 recites that the means for sorting and the means for electrically enhancing the sorting together comprise at least one of: (A) a first filtration device that sorts cells according to their sizes, wherein the first filtration device is succeeded within a fluid flow path by a second filtration device that sorts cells according to their dimensional orientation; or (B) a third filtration device that sorts cells according to their dimensional orientation, wherein the third filtration device is succeeded within the fluid flow path by a fourth filtration device that sorts cells according to their sizes. Accordingly, by providing a third filtration device and a fourth filtration device (instead of a second occurrence of the first filtration device and the second filtration device), the limitations of claim 21 have been made definite while also being incorporated into independent claim 14.

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For these reasons, Applicants respectfully request allowance of claim 14 and withdrawal of the rejections of claim 21-22. Dependent claim 22 is believed to be allowable based on its dependency from patentably distinct independent claim 14.

**Claim Rejections under 35 U.S.C. § 102**

In the Office Action, claims 14, 15 and 18 were rejected under 35 U.S.C. 102(e) as being anticipated by Ohman et al., US Publication 2005/0042766 A1 (the Ohman Publication), by Huang et al., US Patent 7,150,812 (the Huang Patent), and by Austin et al., US Patent 5,427,663 (the Austin Patent).

As explained above, Applicants have amended independent claim 14 by incorporating the subject matter of claim 21 (which was indicated to be allowable if rewritten to overcome a Section 112 rejection and to include the limitations of any base and intervening claims), thereby placing claim 14 in allowable form. Accordingly, Applicants respectfully request allowance of independent claim 14 over the Ohman Publication, the Huang Patent, and the Austin Patent. Dependent claims 15 and 18 are believed to be allowable based on their dependency from patentably distinct independent claim 14.

In the Office Action, claims 1-2 stand rejected as being anticipated by the Austin Patent and by Fisher, US Patent 5,376,878 (the Fisher Patent), while claim 1 also stands rejected as being anticipated by the Huang Patent and by the Ohman Publication.

Applicants have canceled claim 3 and incorporated the subject matter of claim 3 into independent claim 1.

Applicants' independent claim 1 specifies a micro-filtration device for sorting cells comprising an electrode arrangement and an apparatus including a barrier structure defining an array of openings arranged within a fluid flow path. The openings of the barrier structure have at least one of a size and a shape configured to direct a portion of the cells through the openings based on at least one of a size and a shape of each cell. The electrode arrangement is disposed about the array of openings and configured to apply a **non-uniform** electric field to enhance passage of the portion of the cells through the openings. **The electrode arrangement is separate from, and independent of, the barrier structure.**

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First, in the section titled Allowable Subject Matter, paragraph O regarding claim 29 on page 26 of the Office Action acknowledges that the subject matter of claim 29 was allowable over the Ohman Publication, as well as the Huang and Austin Patents. Claim 29 (in combination with the limitations of base claim 23) recites a non-uniform electric field applied within the openings of a barrier structure and that is configured to encourage passage of a portion of cells through the openings. Accordingly, for substantially the same reasons, Applicants respectfully submit that independent claim 1 (as amended to recite a non-uniform electric field) is also patentable over the Ohman Publication, the Huang Patent, and the Austin Patent.

More specifically, with regard to the Huang Patent, the Huang Patent identifies use of an electrophoretic electric field (claim 5). However, the Huang Patent fails to disclose use of a **non-uniform** electric field, as recited in Applicants' independent claim 1.

In addition, the limitation of a non-uniform electric field recited in Applicants' independent claim 1 previously appeared in dependent claim 3 (now canceled). Claim 3 was rejected by the Huang Patent in combination with Noca et al, US Patent 6,685,810 (the Noca Patent). Accordingly, Applicants will address the cited combination of the Huang and Noca Patents in the context of independent claim 1, which now recites a non-uniform electric field.

The Noca Patent generally describes a molecular sieve that uses **electrophoresis**, including one example of an electrophoretic instrument 40 in which an electrophoretic electric field induces a flow of molecules. See Column 4, lines 28-32; Column 10, lines 16-46; and Column 11, lines 5-15. While the Noca Patent mentions a DC field and a pulsed field as possible types of electric fields 64 (see, for example, Column 11, line 58 – Column 12, line 6) and makes limited fleeting references to pulsed fields (see, for example, Column 7, line 5 or claim 27), the Noca Patent fails to clearly teach an electrode arrangement configured to apply a **non-uniform** electric field to enhance passage of a portion of cells through openings of a barrier structure, in the manner recited in Applicants' independent claim 1. Accordingly, one cannot combine the Huang Patent and the Noca Patent and arrive at Applicants' independent claim 1.

For at least these reasons, the Ohman Publication, the Huang Patent, and the Austin Patent each fail to anticipate Applicants' independent claim 1. Moreover, the combination of the Huang Patent and the Noca Patent fails to teach, suggest, or otherwise render obvious

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Applicants' independent claim 1. Accordingly, Applicants respectfully submit that independent claim 1 is allowable over the Ohman Publication, the Huang Patent, and the Austin Patent, as well as the Noca Patent. Dependent claim 4 is believed to be allowable based on its dependency from patentably distinct independent claim 1.

Moreover, as implicitly admitted in the Office Action by the non-application of the Fisher Patent to claim 3, the Fisher Patent apparently fails to teach the use of a non-uniform electric field applied via an electrode arrangement to enhance passage of the portion of cells through openings of a barrier structure, as recited in Applicants' independent claim 1. In general, the Fisher Patent discloses a method to measure a size, number or deformability of a particle based on an aperture impedance principle. See, for example, Column 1, lines 10-15. According to the Fisher Patent, the passage of a particle through an aperture causes a brief change in electrical resistance measured between two electrodes (stationed on opposite sides of the aperture) and a magnitude of the transient resistance is a measure of the size of the particle. See, for example, Column 1, lines 35-38. Passage of the particles through an aperture is induced via flow of a fluid (in which the particles are suspended) applied via a pressure difference. See, for example, Column 5, lines 63-68 and Column 8, lines 37-40.

However, the Fisher Patent fails to address the application of an electric field, and particularly a **non-uniform** electric field, via an electrode arrangement to enhance passage of the portion of cells through openings in a barrier structure, as recited in Applicants' independent claim 1.

For at least these reasons, the Fisher Patent fails to anticipate Applicants' independent claim 1. Accordingly, Applicants respectfully submit that independent claim 1 is allowable over the Fisher Patent. Claim 2 is believed to be allowable based on its dependency from patentably distinct independent claim 1.

In addition, claims 1, 3 and 4 were rejected under 35 U.S.C. 102(e) as being anticipated by Christel et al., US Patent 7,135,144 (the Christel Patent).

Applicants have canceled claim 3, and incorporated the limitations of dependent claim 3 into independent claim 1.

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Among other features, Applicants' independent claim 1 recites that an electrode arrangement is separate from, and independent of the barrier structure that defines the openings through which the portions of cells will pass.

In sharp contrast to Applicants' independent claim 1, the Christel Patent discloses columns within columnar region 16 (Figure 7) or a microcolumnar device (Figure 8) through which cells or particles (suspended within a fluid) will flow under pressure AND in which the columns are made of electrically conductive materials. The conductive columns may optionally be coated with an insulator. See, for example, Column 3, lines 17-20; Column 7, line 65 – Column 8, line 4; Column 7, lines 47-61; and Column 8, lines 57-59. By application of an AC or DC voltage to the conductor (in each column), the particles can be selectively attracted to the insulator surface of the columns. In another example, an AC voltage can be tuned to a frequency that facilitates the attraction and retention of DNA, but not other molecules, to the microstructure. See, for example, Column 8, lines 21-57 and Column 9, lines 7-10.

Accordingly, the Christel Patent teaches that its columns (which define openings through which cells or particles can pass) are conductive to enable application of a voltage across those columns to effect manipulation of cells or particles. This arrangement teaches away from Applicants' independent claim 1, which recites an electrode arrangement that is separate from, and independent of, the barrier structure that defines the openings through which the portions of cells will pass.

In addition, the electrode arrangement of Applicants' claim 1 is configured to apply a non-uniform electric field to enhance **passage** of the portion of cells through the opening of the barrier structure. It is submitted that the Christel Patent also teaches away from this arrangement, as the Christel Patent teaches that its conductive columns attract (and sometimes retain) particles flowing through its columnar structures.

Moreover, while the Christel Patent discloses repelling materials from a surface (of a column) by using an opposite polarity charge, it appears that such repulsion would hinder cells from passing through openings defined between the respective columns of the columnar structures. In any case, the Christel Patent fails to positively teach use of an electrode arrangement (applying a non-uniform electric field) to **enhance passage** of cells through openings of a barrier structure, as recited in Applicants' independent claim 1.

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Applicants further note that in the Office Action, claim 2 was rejected as being made obvious by the Christel Patent and the Noca Patent. Because claim 2 has been canceled and a portion of the limitation from dependent claim 2 has been incorporated into amended independent claim 1, Applicants will address the combination of the Noca Patent and the Christel Patent in the context of independent claim 1.

First, as stated above, the Christel Patent teaches a columnar structure in which each column comprises a conductive element for applying an electric field, which is the direct opposite of Applicants' independent claim 1, in which the electrode arrangement is separate from, and independent of, the barrier structure that defines the openings (through which a portion of cells passes). The Christel Patent uses this columnar structure to manipulate molecules and other particles within a fluid.

Second, on the other hand, the Noca Patent teaches placing electrodes 70 at opposite ends (e.g., proximal and distal ends 46, 48) of a sieve body 44 defining a nano-array sieve (see, for example, Figure 5 and Column 11, lines 58-63). Therefore, the Noca Patent cannot cure this deficiency of the Christel Patent (relative to Applicants' independent claim 1) without destroying the fundamental mechanism of the Christel Patent, which is to manipulate particles via the conductive columns. Accordingly, one of ordinary skill in the art would not attempt to replace the conductive, electrically active feature of the columns of the columnar structure of the Christel Patent with the electrode arrangement (end-placed electrodes 70) of the Noca Patent, and therefore would not arrive at the invention as defined in Applicants' independent claim 1.

Accordingly, the Christel Patent and the Noca Patent fail to teach, suggest, or render obvious Applicants' independent claim 1. Accordingly, Applicants respectfully submit that independent claim 1 is allowable over the combination of the Christel Patent and the Noca Patent.

For at least these reasons, the Christel Patent fails to anticipate Applicants' independent claim 1 and the combination of the Christel and Noca Patents fails to render obvious Applicants' independent claim 1. Accordingly, Applicants respectfully submit that independent claim 1 is allowable over the Christel Patent and/or the Noca Patent.

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Claim 4 is believed to be allowable based on its dependency from patentably distinct independent claim 1. In addition, Applicants note that dependent claim 4 recites that the electrode arrangement is arranged to generate the non-uniform electric field as a temporally varying non-uniform electric field **to move the portion of the cells, after passage through the barrier structure, in a second direction different from the first direction.** In sharp contrast, in the Christel Patent, the columns can attract particles or cells as the cells move through the openings between the columns. However, the columnar structure of the Christel Patent does not cause movement of a portion of cells, after passage through the barrier structure, in a second direction transverse to the first direction (in which cells are moved along the fluid flow path), as recited in Applicants' dependent claim 4. For at least these reasons, the Christel Patent fails to anticipate Applicants' dependent claim 4. Accordingly, Applicants respectfully submit that dependent claim 4 is allowable over the Christel Patent.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 1-4, 14-15, and 18 under 35 U.S.C. § 102.

**Claim Rejections under 35 U.S.C. § 103**

In the Office Action, claim 3 was rejected under 35 U.S.C. 103(a) as being unpatentable over the Huang Patent in view of the Noca Patent. Applicants have canceled claim 3, and incorporated the limitations of claim 3 into independent claim 1. Accordingly, the substance of this rejection has been addressed previously in association with independent claim 1.

In the Office Action, claim 2 was rejected under 35 U.S.C. 103(a) as being unpatentable over the Christel Patent in view of the Noca Patent. Applicants have canceled claim 2, and incorporated certain limitations of claim 2 into independent claim 1. Accordingly, the substance of this rejection has been addressed previously in association with independent claim 1.

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In the Office Action, claim 7 was rejected under 35 U.S.C. 103(a) as being unpatentable over the Christel Patent. Dependent claim 7 is believed to be allowable based on its dependency from patentably distinct independent claim 1.

In the Office Action, claims 23 and 24 were rejected under 35 U.S.C. 103(a) as being unpatentable over the Ohman Publication, Austin Patent, or the Huang Patent.

Applicants note that the rejection of independent claim 23 in the Office Action appears to recite limitations from Applicants' independent claim 14, thereby making the scope of the rejection somewhat unclear. Regardless, Applicants have amended independent claim 23 to incorporate the subject matter of allowable claim 29 (although objected to for being in dependent form), thereby obviating these rejections. Therefore, Applicants respectfully submit that claim 23 is now in allowable form. Dependent claim 24 is believed to be allowable based on its dependency from patentably distinct independent claim 23.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 2-3, 7, and 23-24 under 35 U.S.C. § 103.

**Allowable Subject Matter**

In the Office Action, claims 5, 6, 8-13, 16, 17, 19, 20, and 25-29 were rejected for being dependent upon a rejected base claim, but were indicated to be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims.

Accordingly, Applicants have presented the subject matter of objected to claim 29 in allowable independent form as amended independent claim 23. In addition, Applicants have amended dependent claims 5, 6, 8, 13, 16, 19, 25, and 28 to incorporate the limitations of their base claims and intervening claims, respectively, thereby placing claims 5, 6, 8, 13, 16, 19, 25, and 28 in allowable, independent form. Finally, Applicants also acknowledge with appreciation the indication of the allowable subject matter within the other objected to claims 9-12, 17, 20, and 26-27 that are pending from one of the rewritten allowable independent claims. For these reasons, allowance of claims 5, 6, 8-13, 16, 17, 19, 20 and 23 and 25-28 is respectfully requested.



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**CONCLUSION**

In view of the above, Applicants respectfully submit that pending claims 1, 4-20, and 22-28 are in form for allowance and are not taught or suggested by the cited references. Therefore, reconsideration and withdrawal of the rejections and allowance of claims 1, 4-20, and 22-28 is respectfully requested.

Applicants hereby authorize the Commissioner for Patents to charge Deposit Account No. 08-2025 the amount of \$1,680.00 to cover fees as set forth under 37 C.F.R. 1.16(h)(i).

The Examiner is invited to contact the Applicants' representative at the below-listed telephone numbers to facilitate prosecution of this application.

Any inquiry regarding this Amendment and Response should be directed to either Julia Church Dierker at Telephone No. (248) 649-9900, Facsimile No. (248) 649-9922 or Paul S. Grunzweig at Telephone No. (612) 767-2504, Facsimile No. (612) 573-2005. In addition, all correspondence should continue to be directed to the following address:

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Respectfully submitted,

Winthrop D. Childers et al.

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